CPD article

Histopathology: how to get the best from gastrointestinal biopsies

Sampling of the gastrointestinal tract by endoscopic, or full thickness (open abdominal surgical) biopsy is an invaluable tool in the diagnosis and management of gastrointestinal disease in companion animals. This article gives recommendations on how to collect and submit endoscopic and full thickness biopsies of the gastrointestinal tract, in order to maximise their diagnostic value. It also covers interpretation of the histopathology report and examples of when further samplsing or additional testing may be advisable. It is important to note that these are general recommendations and it is prudent to contact the reporting laboratory with any specific queries or requests.

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Sampling of the gastrointestinal tract by endoscopic or full thickness (open abdominal surgical) biopsy is an invaluable tool in the diagnosis and management of gastrointestinal disease in companion animals. However, the collection of samples requires considerable clinical and surgical skill and a general anaesthetic is needed for the animal, often at significant expense to the owner. For these reasons, it is important to maximise the value of this process by careful case selection, acquisition of high quality biopsy specimens and a clear understanding of both the value and limitations of histological examination. Furthermore, close collaboration between pathologist and clinician is essential, particularly when the histology alone does not provide a definitive diagnosis and further clinical correlation and/or testing is required to obtain a complete picture of the disease process (Elwood, 2005).

Histopathology can provide valuable information to be applied in the management and treatment of gastrointestinal disease, by helping practitioners reach a specific diagnosis or by guiding them in their approach to further investigation and treatment (Stidworthy and Priestnall, 2011). Reaching a definitive diagnosis through histopathology depends on multiple factors, including appropriate case selection, clinical sampling, tissue preparation, and the provision of a relevant and correct clinical history. Nevertheless, each organ system in the body, including the gastrointestinal tract, has a limited repertoire of responses and there will always be cases that present with findings that are not aetiologically-specific, even when sampling and submission have been performed optimally. Therefore, it is important that practitioners and clients understand both the value and limitations of histopathology. The histopathological findings should always be interpreted within the context of the clinical presentation, results of laboratory tests, other diagnostic data and the response to any treatment. This is particularly true for inflammatory conditions of the gastrointestinal tract. The relationship between clinician and pathologist should be open and bidirectional; if the histopathological diagnosis does not fit the patient's clinical presentation, the clinician should not hesitate to contact the pathologist to discuss the case further.

This article provides general outlines and recommendations on how to sample and submit gastrointestinal biopsies. Moreover, it explains the role of the veterinary pathologist in providing a report and explaining how to interpret the results.

When to sample

It is beyond the scope of this article to provide a detailed discussion on appropriate case selection for gastrointestinal biopsy. Gastrointestinal signs are a common presentation and reaching a specific diagnosis can be challenging when the clinical signs are non-specific. Extraintestinal causes of gastrointestinal signs can also be misleading. Gastrointestinal biopsy is generally not warranted in acute gastrointestinal disease, or in cases where the patient is otherwise clinically well and a dietary trial

has not been performed. However, biopsy may be appropriate in cases where there is a history of chronic vomiting and/or diarrhoea in conjunction with either anorexia, severe weight loss, significant blood loss, hypoalbuminaemia, or if there is evidence of an intestinal mass or infiltrative disease on radiographic and/or ultrasonographic examination (Hall, 2019).

Sample types and collection

Before collecting gastrointestinal biopsies, it is important to be aware of the benefits, risks and limitations of endoscopic and full thickness samples (*Table 1* and *2*). In all cases, collection of adequate numbers of samples from multiple locations is highly recommended. For example, submission of an endoscopic biopsy from the stomach for vomiting and diarrhoea may not be as informative as other areas of the gastrointestinal tract. Some lesions may also be segmental (Daniaux et al, 2014) and are more likely to be detected by sampling multiple sites.

Endoscopic biopsies of the gastrointestinal tract can be collected without invasive surgery and a larger area can be surveyed. Although, they are small and superficial, so samples may not be representative of the lesion or may not be a suitable diagnostic for some deeper pathological processes (such as invasion into adjacent tissues) or mural tumours. Endoscopic biopsy forceps should be either disposable or well maintained, and should used with care as they can cause abundant trauma, such as crushing or tearing, precluding detailed examination, making it impossible to assess tissue architecture and cellular detail. Only the mucosa is usually sampled, so multiple samples should be collected from each location (ideally 8–10) to help mitigate for sampling artefacts as well as covering a larger area of the organ. As endoscopic biopsies are difficult to orientate in the tissue block, multiple biopsies improve the likelihood of seeing all features of the tissue sampled. It is best to avoid any unnecessary handling of the samples as they are easily damaged. To achieve this, forceps may be opened directly in the formalin, or the tissue can be gently transferred into a cassette with the help of a needle.

Full thickness biopsies are often superior to endoscopic biopsies as they are less susceptible to collection-related damages and they allow for transmural examination of the gastrointestinal tract, improving the likelihood of reaching a definitive diagnosis. For example, in cats, full thickness biopsies are desirable for the differentiation between inflammation and small-cell lymphoma (Evans et al, 2006; Kleinschmidt et al, 2010). Moreover, all levels

Table 1. Advantages and disadvantages of endoscopic biopsies

Advantages	Disadvantages
Less invasive	Requires practice to collect diagnostic samples
Lower risk of complications	Risk of gastrointestinal perforation if inexperienced surgeon or if tissue is particularly friable/ inflamed/ damaged
Multiple areas of mucosa can be sampled	Samples often subject to artefacts
Mucosal appearance can be evaluated	Some areas of the gastrointestinal tract may be out of reach
	Requires purchase of specific equipment

Table 2. Advantages and disadvantages of full-thickness (open abdominal surgical) biopsies

Advantages	Disadvantages
Better quality samples with fewer artefacts	More invasive
Larger amount of tissue to be examined	Higher risk of complications (Swinbourne et al, 2017)
Allows evaluation of the entire gastrointestinal wall (submucosa, tunica muscularis and serosa)	May miss focal mucosal lesions
All areas of the gastrointestinal tract can be sampled	Can only examine serosal surfaces
Inspection/sampling of other organs is also possible	

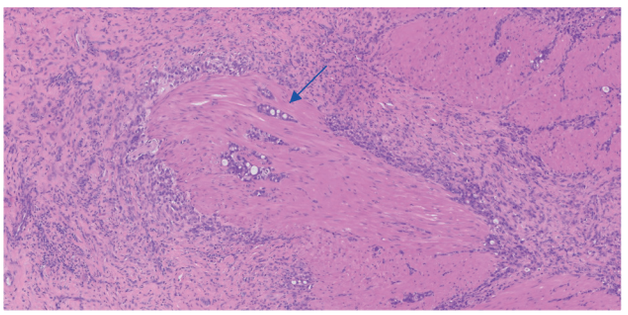

Figure 1. Laparotomic biopsies of gastric carcinoma. The mass is located primarily in the tunica muscularis and would not be captured in endoscopic biopsies. Blue arrow indicates neoplastic cells at the level of the tunica muscularis which were not found within the mucosa. Haematoxylin and eosin stain at 10x.

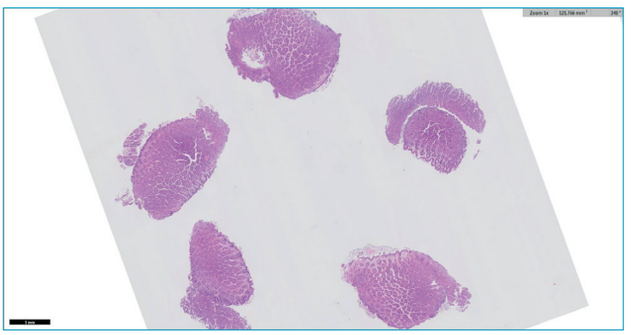

Figure 2. Endoscopic biopsies of stomach. Endoscopic biopsies are often tiny and difficult to orientate in the tissue block. They are often captured in various planes of section. Submitting multiple biopsies increases the likelihood of visualising all levels of the tissue. Haematoxylin and eosin stain at 1x.

of the intestinal wall can be examined (mucosa, submucosa, muscularis and serosa) rather than just the mucosa and it also enables evaluation of invasion (*Figure 1*). Although, this type of biopsy still may miss a focal lesion.

Sample quality

The sensitivity and specificity of histopathology as a diagnostic modality is heavily influenced by sample quality. Therefore, the collection of adequate numbers of high-quality representative samples is essential to making a diagnosis (*Figure 2*). It is important to avoid the common causes of artefactual changes, including crushing the tissue with forceps, stretching the tissue during sampling, delaying fixation, coagulating the tissue with electrocautery and allowing small biopsies to dry out on gauze and/or under surgical lamps. Some examples of good quality and bad quality samples are illustrated in *Figures 3-8*.

In some cases, samples may be of limited diagnostic value or non-diagnostic. Some of the most common causes of non-diagnostic samples, and suggestions for mitigating for them, are summarised in *Table 3*.

Clinical history and signalment

Providing a complete signalment and relevant clinical history is crucial for the interpretation of the biopsy samples, as blinded examination may significantly impact the results (Stidworthy and Priestnall, 2011). The information required for optimal

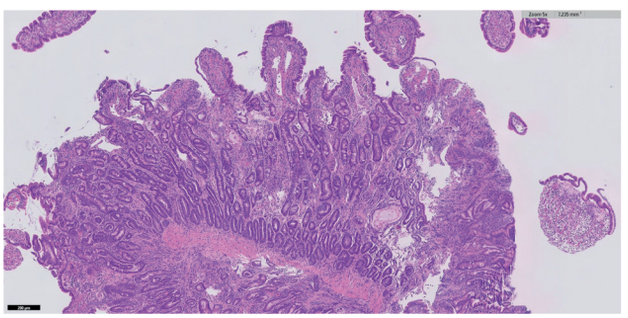

Figure 3. Good quality endoscopic biopsy. This sample has numerous villous profiles (at least three is recommended) and encompasses the entire depth of the intestinal mucosa extending to the muscularis mucosae. Haematoxylin and eosin stain at 5x.

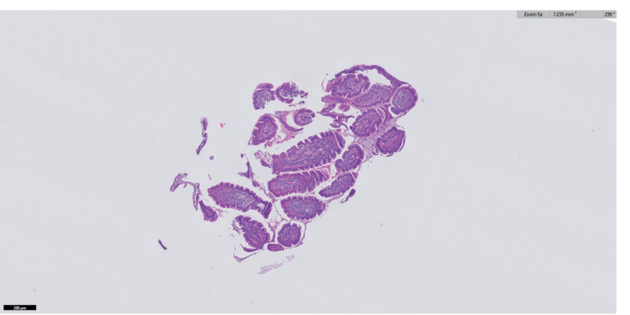

Figure 4. Poor quality endoscopic biopsy. This sample of duodenum only shows the villus tips (superficial sections) and is considered inadequate for interpretation. Haematoxylin and eosin stain at 5x.

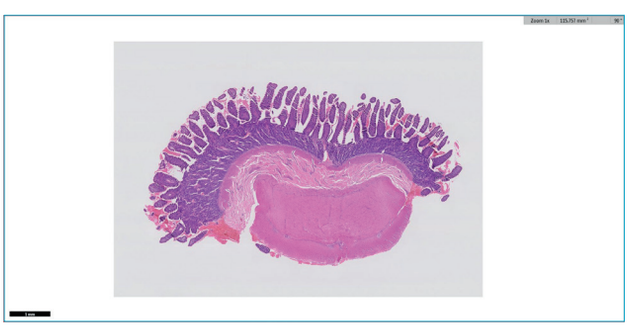

Figure 5. Good quality full thickness biopsy. The sample shows all layers of the gastrointestinal wall (from mucosa to serosa). Haematoxylin and eosin stain at 1x.

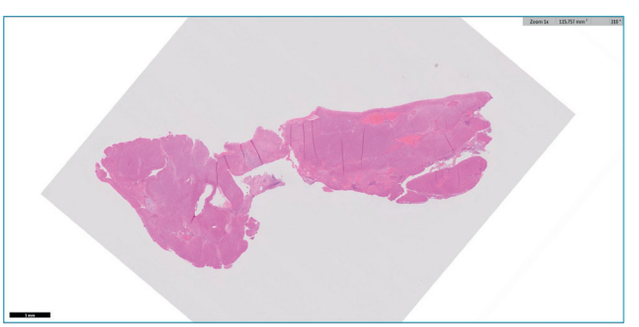

Figure 6. Poor quality full thickness biopsy. This sample only shows the tunica muscularis, owing to an inappropriate surgical technique, and is therefore considered non-diagnostic. Haematoxylin and eosin stain at 1x.

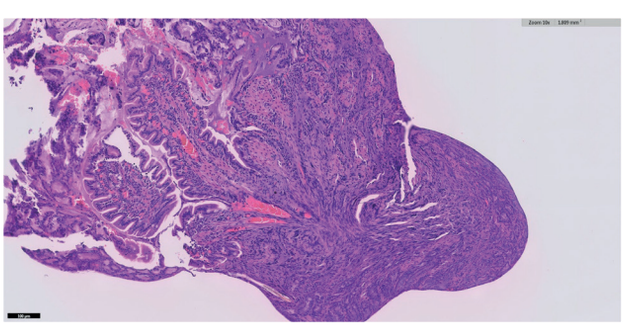

Figure 7. Crush artefact in an endoscopic biopsy. There is abundant crush artefact with loss of architecture and cellular detail making the sample non-diagnostic. Haematoxylin and eosin stain at 10x.

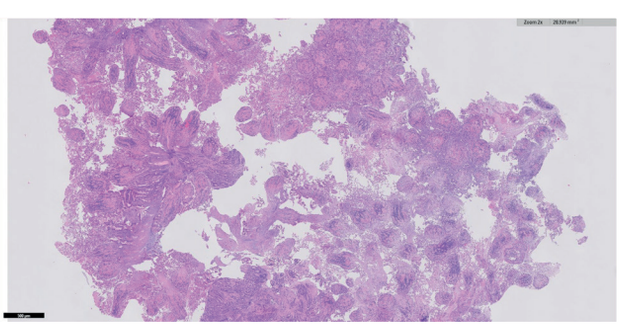

Figure 8. Highly necrotic sample. There is diffuse necrosis with no evidence of normal tissue or pathology and therefore a diagnosis cannot be provided. Haematoxylin and eosin stain at 2x.

Table 3. Common causes of poor quality or non-diagnostic samples

Issue	Explanation	Solution
Non-representative samples	• Superficial samples (just surface epithelium or villus tips) • Too few samples from each location • Not all affected locations have been sampled • The lesion is deeper than the biopsy	• Take samples from the most representative area of the lesion • If multiple lesions, take multiple samples of each lesion when possible • Take multiple samples from each part of the gastrointestinal tract • Include as many segments of the gastrointestinal tract as possible • Consider taking laparotomic biopsies
Necrotic endoscopic biopsies	• Ulcerated or necrotic area may yield no viable tissue for examination	• Obtain samples that include the junction of normal and abnormal • Consider taking laparotomic biopsies which are larger and including all layers of the wall • Submit multiple samples of the same lesion to maximise chance of collecting viable tissue
Necrotic incisional biopsies of masses	• Incisional biopsy of a large tumour may capture only central necrosis	• Avoid necrotic and haemorrhagic areas • Take multiple samples of the mass at different levels • Sample the periphery of the mass
Autolysed excisional biopsies of masses	• Large masses are slow to fix resulting in central autolysis and a non-diagnostic sample	• If the mass is very large, consider sectioning the mass for better fixation • Ink margins or place sutures so they are identifiable and provide a diagram so the tissue can be reconstructed in the laboratory and margins correctly identified
Artefactual changes associated with endoscopic biopsies	• Endoscopic biopsies are small and susceptible to crush and stretch artefact, dehydration under surgical lamps and poor orientation	• Take multiple samples from the same site • Biopsy forceps should be well maintained and handled with care or disposable forceps can be used to avoid maintenance • Avoid any unnecessary handling of the specimens • Place samples in formalin as soon as they are collected

interpretation of gastrointestinal biopsies is similar to that required for other organ systems.

- **Signalment**. This includes species, breed, gender and age. This is important as some pathological processes are more common or specific to a particular species, breed, age range or gender.
- **Clinical history**. This information is essential in formulating differential diagnoses, as well as answering any specific questions and concerns the clinician may have about the case. The clinical history should include the clinical signs, diagnostic imaging/laboratory findings, relevant treatments and any response to therapy. Simply providing the patient's entire clinical history directly from the practice management software is not advisable because it can take a great deal of time to locate the relevant information, which risks it being overlooked by the pathologist. Details regarding the type and length of treatment, and the animal's response to it, are important as they may affect the histological appearance (such as corticosteroids, which can affect the amount of inflammation seen in gastrointestinal biopsies and non-steroidal anti-inflammatories can cause gastrointestinal ulcers). In some cases, where possible, it may be advisable to stop a treatment for a period of time before sampling. If unsure of the time frame, please contact the pathologist before submission. Other information such as concomitant diseases may also be relevant. It is also highly recommended that the clinician's differentials diagnoses are stated on the submission form.
- **Site/location**. This is particularly important for gastrointestinal biopsies as some segments of the intestinal tract can be difficult to differentiate histologically, particularly if diseased. Submission of samples in separate labelled containers/cassettes is highly recommended. This applies to both full thickness and endoscopic biopsies. Moreover, if specific lesions are sampled, labelling of the sample with the word "lesion" and the location is recommended as there may be no normal tissue to enable the sample site to be identified.
- **Type of sample/biopsy**. Indicate the type of samples you are sending. The most common options for the gastrointestinal tract are endoscopic biopsy and full thickness biopsy. Localised lesions should be described as excisional biopsies (fully excised) or incisional biopsies (partially excised). This information is necessary for the interpretation of margins.
- **Other information and clinical data**. Colour photographs and laboratory results can be helpful in the interpretation of clinical and/or histopathological findings. Laboratory results can be summarised with the clinical history.

Sample submission

Contacting the laboratory for instructions regarding sample submission is recommended because there can be variety in the preferred method. In all cases (including gastrointestinal samples) the sample(s) should be representative of the lesion/process, as well as being properly fixed and with as little artefactual damage as possible.

All containers should be labelled (including patient name/number and site submitted). The formalin to tissue ratio should be 10:1. Features such as colour, size or shape of the specimen are unreliable methods of identifying samples as these may change during fixation. Samples from different sites are best submitted in separate labelled containers or within separately labelled cassettes in the same container. Labelling cassettes with a pencil or permanent marker is recommended as other marking tools may be erased in formalin (*Figures 9-11*).

Small tissue samples

Small tissue samples (such as small full-thickness biopsies or endoscopic biopsies) should be submitted in a small container. When possible, endoscopic biopsies are best submitted in cassettes labelled with pencil or permanent marker. If cassettes are not available, samples can be submitted floating in formalin, but in different containers for the different sites. If this is the case, please include the number of samples taken on the submission form, to ensure that they are all included in the histopathological examination. It is best to avoid the use of cardboard or gauze as the tissue may get dehydrated or damaged (Ruiz et al, 2016).

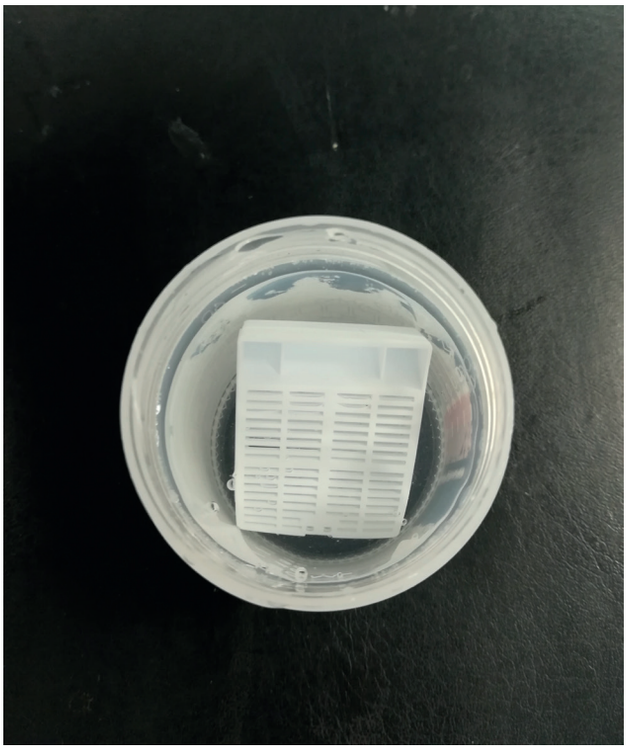

Figure 10. The photograph shows a sample container with a cassette submerged in formalin.

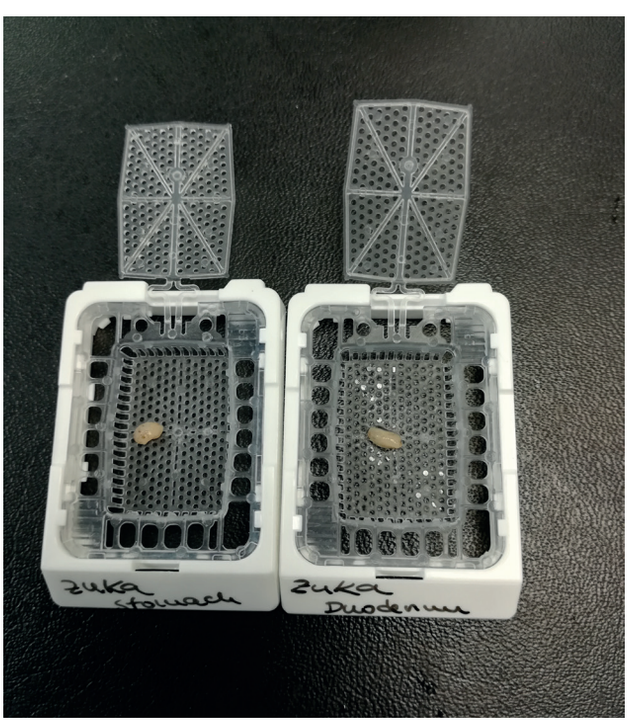

Figure 9. The photograph shows two opened cassettes with endoscopic biopsy samples of stomach and duodenum on mesh inserts.

Figure 11. The photograph shows a clearly-labelled sample container with endoscopic biopsies submitted free-floating in formalin. Labelling both the lid and container is recommended.

Particularly for endoscopic biopsies, it is important to collect multiple samples from each site and avoid unnecessary handling as these small samples tend to present with more artefactual changes.

Large tissue samples

For larger tissue samples (such as a segment of the gastrointestinal tract) there are several options for submission, each of which have their benefits and drawbacks. Individual practices and laboratories will likely differ in their preferred method.

- The sample may be submitted whole, either submerged in formalin or wrapped in formalin-soaked gauze after it has fixed at the practice. This method retains the integrity of the lesion and the surgical margins. However, it requires a larger container and increased volume of formalin. It may not provide optimal fixation as the formalin takes time to penetrate a large specimen, which may continue to undergo autolysis. It is essential that the specimen reaches the laboratory as soon as possible so that it may be sampled and fully fixed (if necessary) to avoid further autolysis.
- The entire sample may be submitted in several sections to improve fixation and allow samples to be sent in multiple smaller containers. These must be carefully labelled, with sutures and/or tissue ink so that the specimen can be correctly reconstructed in the laboratory to allow correct sampling and accurate identification of surgical margins. A clear diagram should always be provided on the submission form.
- Representative samples of the specimen may be submitted. This provides optimal fixation but relies on the person sampling to correctly identify and collect the most appropriate samples. These should include the mass/lesion and the junction between normal and affected tissue (approximate size of the piece being 2x2x1 cm). It may also be appropriate to collect samples from the surgical margins (oral, aboral or mesenteric) if they are not included in the samples described above, as well as any associated lymph nodes. A clear diagram of the full specimen illustrating the location of the lesion(s) and any samples collected should be provided on the submission form. Samples should be submitted in separate containers and clearly labelled. Areas of haemorrhage and necrosis should be avoided as they are often of limited diagnostic value. It is also recommended to save any remaining tissue (fixed in formalin) until the final report is received, in case additional samples are required. Keeping fresh tissue, microbial swabs, and/or content in the fridge is also recommended in case further testing is required.

The histopathological report

In general, the aims of the pathologist are to distinguish normal from diseased tissue, to characterise the severity of the changes and to provide a diagnosis to facilitate prognosis and appropriate treatment. Reports from different laboratories may vary in style, but contents should be similar and should include:

- Brief clinical history and signalment summarised from the information provided on the submission form.
- Histological description of what is observed in the sections of tissue examined.
- Diagnosis, which is an interpretation of the histopathological findings (for example, lymphoplasmacytic enteritis). Occasionally, this may also be consistent with a name of the disease (for example, granulomatous enteritis with Periodic acid-Schiff positive macrophages consistent with histiocytic ulcerative 'granulomatous' colitis). Alternatively, an aetiological diagnosis may be provided (such as parvoviral enteritis). In this section, the severity of disease will also be reported.
- Comment, which usually provides an explanation of the diagnosis and what it may imply in terms of prognosis, prevalence of the disease and possible recurrence. If a definitive cause and diagnosis are not reached, possible differential diagnoses will be provided. Suggestions for further tests/sampling may also be included. In the case of malignant neoplasia, a grade (where possible) is provided in addition to information such as survival time, metastatic rate and possible metastatic sites. If the sample is non-diagnostic, the explanation for this should also be clarified. The length and detail of the comment will vary from case to case and between pathologists and different laboratories.
- Signature and name of the reporting pathologist will be provided at the end of the report, including their contact details should you wish to discuss the case further.

The diagnostic report is based on the samples examined in the context of the clinical history, signalment information and other diagnostic data provided. While it may include information regarding the likely prognosis, progression of disease and recommendations for further sampling or monitoring, in general the report will not provide specific information regarding treatment or clinical management of the case.

Further sampling and ancillary testing

In some cases, further sampling and/or additional ancillary testing are recommended. This may be because a definitive diagnosis cannot be reached from the initial section(s), or that further testing could provide further information regarding the likely prognosis and/or response to treatment. Particular care should be taken in differentiating some gastrointestinal inflammatory processes from intestinal lymphoma, especially when only endoscopic biopsy specimens are available for evaluation. Resampling or full thickness biopsies may be recommended (Evans et al, 2006; Kleinschmidt et al, 2010).

Other common reasons which may warrant resampling have been covered above, but include insufficient samples (too few, too small, too superficial, or not all sites included), sampling artefact, massive ulceration and/or necrosis, or non-representative samples. Further sampling and ancillary tests include:

- Additional 'deeper levels' from the existing processed tissue or preparing additional sections from the remaining 'wet' tissue.
- 'Special stains' for infectious agents (such as Gram for bacteria and Periodic acid-Schiff for fungi), cytoplasmic granules/pigment (toluidine blue for mast cell granules), and extracellular matrix components (Masson's trichrome for fibrous tissue).
- Immunohistochemical testing, which involves the use of antibodies to detect specific epitopes. This is commonly used for immunophenotyping lymphomas and providing a World

Health Organization classification (B and T cell markers). Immunohistochemistry can also be used to help further characterise poorly differentiated tumours, detect infectious agents and assess the proliferation index of a tumour (such as Ki67 testing for mast cell tumours (Scase et al, 2006).

- Molecular/genetic analysis. This can be used for clonality testing (polymerase chain reaction for antigen receptor rearrangements) in cases where it is difficult to differentiate histologically between florid lymphocytic inflammation and lymphoid neoplasia. Typical examples would be differentiating between enteritis and lymphoma in cats (Kiupel et al, 2011). However, this technique is not always definitive (Marsilio et al, 2019). For such cases, a recently reported option is histology guided mass spectrometry. At the time of writing, this technique is only available in the US (Marsilio et al, 2020). Molecular testing can also be used to identify specific mutations, which may provide further information regarding prognosis and response to treatment (such as exon 8 and 11 in the *c-kit* gene for mast cell tumour) (Marconato et al, 2014). Finally, specific pathogenic bacteria may be detected through the use of fluorescence in situ hybridisation (Simpson et al, 2006; Maunder et al, 2016).

Interpretation of histopathology reports and reporting method for endoscopic biopsies

All histopathology reports follow a standard format, including the diagnosis, clinical history, histology and comment, as described above. Some laboratories may also include additional subheadings such as prognosis and margins. However, gastrointestinal endoscopic biopsies in dogs and cats follow the standardised World Small Animal Veterinary Association (WSAVA) reporting method. The WSAVA Gastrointestinal Standardisation Group was established to develop endoscopic and microscopical standards in small animal gastroenterology (Day et al, 2008). Although some pathological diagnoses can be made relatively easily (such as large cell lymphoma), interpretation of inflammatory changes is complex and to some extent, subjective. Before the WSAVA method, reports had highlighted the lack of uniformity in up to 50% of enteric biopsy reports (Willard et al, 2001). This interpretative variation can impact the clinical diagnosis, prognosis, treatment and value of follow-up biopsies.

The WSAVA group developed a template of the major histopathological changes that occur during inflammatory disease of the canine and feline stomach (body, antrum and pylorus), duodenum and colon. It also established a set of standardised criteria and a reporting method for endoscopic biopsies. However, no standardised WSAVA criteria have been provided for the jejunum, ileum and caecum. In the WSAVA method, rather than providing a paragraph describing the histological findings, the report focuses on specific architectural and inflammatory features that are informative in reaching a morphologic diagnosis. This is usually presented as a series of short sentences each of which are graded as normal, mild, moderate or severe. Some pathologists may also choose to include a short description for each organ examined, but this is optional. A diagnosis and a comment will be provided in the usual manner.

Gastrointestinal inflammation and inflammatory bowel disease/chronic inflammatory enteropathy

One of the most common histopathological changes within the gastrointestinal tract is the presence of inflammation. However, there is a general misconception that a histopathological diagnosis of inflammation (such as enteritis) equates to inflammatory bowel disease (IBD), also known as chronic inflammatory enteropathy. Chronic enteropathy and IBD are broad terms, often used interchangeably, encompassing a range of complex clinical syndromes. These include steroid-responsive enteropathy, immunosuppressant-responsive enteropathy and food-responsive enteropathy, the precise definitions of which, and relationships between, remain the subject of debate. However, regardless of the nomenclature used, these are clinical syndromes for which it is difficult to develop an objective histopathological counterpart (Uzal et al, 2016). A histopathological diagnosis of gastritis, gastroenteritis, gastroenterocolitis, enteritis, enterocolitis or colitis refers to the presence of an inflammatory process within the different levels of the gastrointestinal tract, but this does not imply that IBD/chronic enteropathy is the clinical disease. Inflammation within the gastrointestinal tract may be caused by a wide range of other factors including dietary/hypersensitivity reactions, aberrant responses to luminal microflora, foreign bodies, drugs (non-steroidal anti-inflammatories), motility disorders and underlying systemic disease. Chronic enteropathy/IBD should only be considered after all these alternatives have been ruled out. In summary, it is not appropriate for a pathologist to diagnose IBD/chronic enteropathy, but instead describe the histological changes and, where appropriate, indicate that they may be compatible with the syndrome. Please note that a clinical diagnosis of IBD/chronic enteropathy requires chronic gastrointestinal signs (for more than

KEY POINTS

- Sampling of the gastrointestinal tract by endoscopic or full thickness (open abdominal surgery) biopsy is an invaluable tool in the diagnosis and management of gastrointestinal disease in companion animals.
- It is important to maximise the value of this process by careful case selection, acquiring high quality biopsy specimens and having a clear understanding of both the value and limitations of histological examination.
- Close collaboration between pathologist and clinician is essential, particularly when the histology alone does not provide a definitive diagnosis and further clinical correlation and/or testing is required.
- The sensitivity and specificity of histopathology as a diagnostic modality is heavily influenced by sample quality and therefore the collection of adequate numbers of high-quality representative samples is essential to making a diagnosis.
- Histopathology reports for gastrointestinal endoscopic biopsies in dogs and cats follow the standardised World Small Animal Veterinary Association method, based on an established set of standardised criteria, which improves consistency between pathologists and maximises the value of initial and follow-up biopsies.

3 weeks), histopathological evidence of inflammation, inability to document other causes of inflammation by a thorough diagnostic evaluation and an inadequate response to treatment trials (dietary, antibacterial, anthelmintic), as well as a clinical response to anti-inflammatory or immunosuppressive agents. Histopathological changes in the absence of these criteria do not allow a diagnosis of IBD/chronic enteropathy to be made (Washabau et al, 2010).

Allenspach et al (2019) have recently described a scoring system to correlate histopathological changes with clinical activity in dogs with IBD. If requested, pathologists may be able to provide a score based on this system and correlate it with the reported clinical findings.

Conclusions

Sampling of the gastrointestinal tract by endoscopic or full thickness biopsy is an invaluable tool in the diagnosis and management of gastrointestinal disease in companion animals. Reaching a definitive histopathological diagnosis is dependent on many factors, including appropriate sampling, tissue preparation, and the provisision of a complete and correct clinical history. It is also significantly improved by good communication between the attending clinician and the pathologist. The gastrointestinal tract is composed of several large organs and in many cases only small sections are submitted, so sampling multiple sites is highly recommended. Endoscopic biopsies of the stomach, duodenum and colon should be evaluated using the standardised WSAVA method. In general, the diagnosis should be interpreted in the context of the clinical presentation, clinical examination findings, other diagnostic data and any response to treatment. In some cases, resampling and/or further testing may be warranted.

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Conflicts of interest

The authors declare no conflicts of interest.

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